

WHAT IS CLAIMED IS:

- 1 1. An isolated infectious chimeric respiratory syncytial virus (RSV)
2 comprising a major nucleocapsid (N) protein, a nucleocapsid phosphoprotein (P), a large
3 polymerase protein (L), a RNA polymerase elongation factor, and a partial or complete
4 RSV background genome or antigenome of a human or bovine RSV combined with one
5 or more heterologous gene(s) and/or genome segment(s) of a different RSV to form a
6 human-bovine chimeric RSV genome or antigenome.
- 1 2. The chimeric RSV of claim 1, wherein said one or more
2 heterologous gene(s) and/or genome segment(s) include one or more RSV NS1, NS2, N,
3 P, M, SH, M2(ORF1), M2(ORF2), L, F or G gene(s) or genome segment(s) or a leader,
4 trailer or intergenic region of the RSV genome or a segment thereof.
- 1 3. The chimeric RSV of claim 2, wherein said one or more
2 heterologous gene(s) and/or genome segment(s) includes one or more gene(s) or genome
3 segment(s) encoding a RSV F, G and/or SH glycoprotein or an immunogenic domain or
4 epitope thereof.
- 1 4. The chimeric RSV of claim 1, wherein the human-bovine chimeric
2 RSV genome or antigenome encodes a chimeric glycoprotein having both human and
3 bovine glycoprotein domains or immunogenic epitopes.
- 1 5. The chimeric RSV of claim 4, wherein said one or more
2 heterologous gene(s) and/or genome segment(s) includes a gene segment encoding a
3 glycoprotein ectodomain.
- 1 6. The chimeric RSV of claim 1, wherein a heterologous gene or
2 genome segment is substituted for a counterpart gene or genome segment in a partial RSV
3 background genome or antigenome.
- 1 7. The chimeric RSV of claim 1, wherein a heterologous gene or
2 genome segment is added adjacent to, within, or as a replacement to, a noncoding region
3 of the partial or complete RSV background genome or antigenome.

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8. The chimeric RSV of claim 1, wherein a heterologous gene or genome segment is added or substituted at a position corresponding to a wild-type gene order position of a counterpart gene or genome segment within the partial or complete RSV background genome or antigenome.

9. The chimeric RSV of claim 1, wherein a heterologous gene or genome segment is added or substituted at a position that is more promoter-proximal or promoter-distal compared to a wild-type gene order position of a counterpart gene or genome segment within the partial or complete RSV background genome or antigenome.

10. The chimeric RSV of claim 1, wherein the chimeric genome or antigenome comprises a partial or complete human RSV background genome or antigenome combined with one or more heterologous gene(s) and/or genome segment(s) from a bovine RSV.

11. The chimeric RSV of claim 10, wherein one or more genes selected from N, P, NS1, NS2, M2-1 and M of a human RSV is/are replaced by one or more heterologous gene(s) from a bovine RSV.

12. The chimeric RSV of claim 11, wherein both N and P genes of a human RSV are replaced by counterpart N and P genes from a bovine RSV.

13. The chimeric RSV of claim 11, wherein both NS1 and NS2 genes of a human RSV are replaced by counterpart NS1 and NS2 genes from a bovine RSV.

14. The chimeric RSV of claim 11, wherein two or more of the M2-1, M2-2 and L genes are replaced by counterpart genes from a bovine RSV

15. The chimeric RSV of claim 11, wherein each of the N, P, NS1, NS2, M2-1 and M genes of a human RSV are replaced by counterpart N, P, NS1, NS2, M2-1 and M genes from a bovine RSV.

16. The chimeric RSV of claim 1, wherein the chimeric genome or antigenome comprises a partial or complete bovine RSV background genome or antigenome combined with one or more heterologous gene(s) and/or genome segment(s) from a human RSV.

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1 17. The chimeric RSV of claim 16, wherein one or more human RSV
2 glycoprotein genes selected from F, G and SH, or one or more genome segment(s)
3 encoding cytoplasmic domain, transmembrane domain, ectodomain or immunogenic
4 epitope portion(s) of F, G, and/or SH is/are added or substituted within a partial or
5 complete bovine RSV background genome or antigenome.

1 18. The chimeric RSV of claim 17, wherein one or both human RSV
2 glycoprotein genes F and G is/are substituted to replace one or both counterpart F and G
3 glycoprotein genes in a partial bovine RSV background genome or antigenome.

1 19. The chimeric RSV of claim 17, wherein the human-bovine
2 chimeric genome or antigenome incorporates antigenic determinants from one or both
3 subgroup A and subgroup B human RSV.

1 20. The chimeric RSV of claim 17, wherein both human RSV
2 glycoprotein genes F and G are substituted to replace counterpart F and G glycoprotein
3 genes in the bovine RSV background genome or antigenome.

1 21. The chimeric RSV of claim 20, which is rBRSV/A2.

1 22. The chimeric RSV of claim 9, wherein one or more human RSV
2 glycoprotein genes selected from F, G and SH is/are added or substituted at a position that
3 is more promoter-proximal compared to a wild-type gene order position of a counterpart
4 gene or genome segment within a partial or complete bovine RSV background genome or
5 antigenome.

1 23. The chimeric RSV of claim 22, wherein both human RSV
2 glycoprotein genes G and F are substituted at gene order positions 1 and 2, respectively,
3 to replace counterpart G and F glycoprotein genes deleted at wild type positions 7 and 8,
4 respectively in a partial bovine RSV background genome or antigenome.

1 24. The chimeric RSV of claim 23, which is rBRSV/A2-G1F2

1 25. The chimeric RSV of claim 17, wherein the chimeric genome or
2 antigenome is further modified by addition or substitution of one or more additional
3 heterologous gene(s) or genome segment(s) from a human RSV within the partial or

1 54. The method of claim 48, wherein the chimeric RSV elicits an
2 immune response against both human RSV A and RSV B.

1 55. The method of claim 48, wherein the chimeric RSV elicits an
2 immune response against either human RSV A or RSV B and is co-administered with an
3 immunologically sufficient amount of a second attenuated RSV capable of eliciting an
4 immune response against human RSV A or RSV B, whereby an immune response is
5 elicited against both human RSV A and RSV B.

1 56. The method of claim 55, wherein the chimeric RSV and second
2 attenuated RSV are administered simultaneously as a mixture.

1 57. An immunogenic composition to elicit an immune response against
2 RSV comprising an immunologically sufficient amount of the chimeric RSV of claim 1 in
3 a physiologically acceptable carrier.

1 58. The immunogenic composition of claim 57, formulated in a dose of
2 10^3 to 10^6 PFU.

1 59. The immunogenic composition of claim 57, formulated for
2 administration to the upper respiratory tract by spray, droplet or aerosol.

1 60. The immunogenic composition of claim 57, wherein the chimeric
2 RSV elicits an immune response against either human RSV A or RSV B.

1 61. The immunogenic composition of claim 57, wherein the chimeric
2 RSV elicits an immune response against both human RSV A and RSV B

1 62. The immunogenic composition of claim 57, wherein the chimeric
2 RSV elicits an immune response against either human RSV A or RSV B and wherein the
3 composition further comprises an immunologically sufficient amount of a second
4 attenuated RSV capable of eliciting an immune response against human RSV A or RSV
5 B, whereby the composition elicits an immune response against both human RSV A and
6 RSV B.

1 63. An isolated polynucleotide molecule comprising a chimeric RSV
2 genome or antigenome which includes a partial or complete RSV background genome or

3 antigenome of a human or bovine RSV combined with one or more heterologous gene(s)
4 or genome segment(s) of a different RSV to form a human-bovine chimeric RSV genome
5 or antigenome.

1 64. The isolated polynucleotide of claim 63, wherein said one or more
2 heterologous gene(s) and/or genome segment(s) include one or more RSV NS1, NS2, N,
3 P, M, SH, M2(ORF1), M2(ORF2), L, F or G gene(s) or genome segment(s) or a leader,
4 trailer or intergenic region of the RSV genome or a segment thereof.

1 65. The isolated polynucleotide of claim 63, wherein a heterologous
2 gene or genome segment is substituted for a counterpart gene or genome segment in a
3 partial RSV background genome or antigenome.

1 66. The isolated polynucleotide of claim 63, wherein a heterologous
2 gene or genome segment is added adjacent to, within, or as a replacement to, a noncoding
3 region of the partial or complete RSV background genome or antigenome.

1 67. The isolated polynucleotide of claim 63, wherein a heterologous
2 gene or genome segment is added or substituted at a position that is more promoter-
3 proximal or promoter-distal compared to a wild-type gene order position of a counterpart
4 gene or genome segment within the partial or complete RSV background genome or
5 antigenome.

1 68. The isolated polynucleotide of claim 63, wherein the chimeric
2 genome or antigenome comprises a partial or complete human RSV background genome
3 or antigenome combined with one or more heterologous gene(s) and/or genome
4 segment(s) from a bovine RSV.

1 69. The isolated polynucleotide of claim 68, wherein one or more
2 genes selected from N, P, NS1, NS2, M2-1 and M of a human RSV is/are replaced by one
3 or more heterologous gene(s) from a bovine RSV.

1 70. The isolated polynucleotide of claim 68, wherein both N and P
2 genes of a human RSV are replaced by counterpart N and P genes from a bovine RSV.

3 to replace counterpart G and F glycoprotein genes deleted at wild type positions 7 and 8,
4 respectively in a partial bovine RSV background genome or antigenome.

1 79. The isolated polynucleotide of claim 73, wherein the chimeric
2 genome or antigenome is further modified by addition or substitution of one or more
3 additional heterologous gene(s) or genome segment(s) from a human RSV within the
4 partial or complete bovine background genome or antigenome to increase genetic stability
5 or alter attenuation, reactogenicity or growth in culture of the chimeric virus.

1 80. The isolated polynucleotide of claim 73, wherein one or more
2 human RSV envelope-associated genes selected from F, G, SH, and M is/are added or
3 substituted within a partial or complete bovine RSV background genome or antigenome.

1 81. The isolated polynucleotide of claim 80, wherein human RSV
2 envelope-associated genes F, G, and M are added within a partial bovine RSV
3 background genome or antigenome in which envelope-associated genes F, G, SH, and M
4 are deleted.

1 82. The isolated polynucleotide molecule of claim 63, wherein the
2 human-bovine chimeric genome or antigenome incorporates antigenic determinants from
3 both subgroup A and subgroup B human RSV.

1 83. The isolated polynucleotide molecule of claim 63, wherein the
2 chimeric genome or antigenome is further modified by incorporation of one or more
3 attenuating mutations.

1 84. The isolated polynucleotide molecule of claim 63, further
2 comprising a nucleotide modification specifying a phenotypic change selected from a
3 change in growth characteristics, attenuation, temperature-sensitivity, cold-adaptation,
4 plaque size, host-range restriction, or a change in immunogenicity.

1 85. The isolated polynucleotide molecule of claim 63, wherein a SH,
2 NS1, NS2, M2ORF2, or G gene is modified.

1 86. The isolated polynucleotide molecule of claim 85, wherein the SH,
2 NS1, NS2, M2 ORF2, or G gene is deleted in whole or in part or expression of the gene is
3 ablated by introduction of one or more stop codons in an open reading frame of the gene.

